

REMARKS

Reconsideration and reexamination of this application are respectfully requested.

A. Status of the Claims

Claims 27, 28, 33-49, and 66-76 are cancelled herein without prejudice or disclaimer to the presentation of the same or similar claims in continuation and divisional applications.

Claims 65, 77-79, and 82 are amended. The amendment to claim 65 combines the conditions recited in canceled claim 27 with those previously recited in claim 65, as in claim 27 prior to the previous amendment. Claim 65 still reads on the invention elected in the response to restriction requirement filed May 9, 2008, which was Group I, Claims 27-28 and 33-49, drawn to a method for the treatment of cardiac insufficiency, myocardial infarct and/or angina pectoris comprising administering to a patient in need thereof a fumaric acid derivative. The amended claims also read on the species elected in that response, namely myocardial infarct, which is a species of cardiac insufficiency, and the species fumaric acid dimethyl ester, which is a species of formula I (fumaric acid dialkyl esters).

The amendment to claim 65 also specifies that the pharmaceutical preparation administered comprises dimethyl fumarate, methyl hydrogen fumarate, or a combination thereof.

The amendments to claims 77-79 and 82 conform the language of those claims to that of amended claim 65.

New claims 85-88 are also added.

With entry of this amendment claims 65 and 77-88 are pending, of which claim 84 has been withdrawn as directed to a nonelected invention. Applicant respectfully requests that claim 84 be rejoined and examined with claim 65 upon a finding that claim 65 is allowable.

All of the amended and new claims are fully supported by the application as filed and do not introduce new matter.

B. Obviousness Rejection

Claims 65, 66, 68, 69, and 74-83 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Pye et al., *Am. J. Physiol. Heart Circ. Physiol.*, Vol. 284, pp. 919-26 (2002) ("Pye") in view of Joshi et al., WO 02/055067 ("Joshi"). Action at pages 3-4.

The Examiner characterizes Pye as "disclos[ing] treatment of patients during myocardial infarction with NFkappaB inhibitors, which was shown to decrease the amount of reperfusion injury (p. 925, column 2, lines 41-44)." Action at page 4. The Examiner acknowledged that Pye "differs from the instant claims insofar as it does not disclose the use of fumaric acid derivatives." Action at page 4.

The Examiner characterizes Joshi as "disclos[ing] the use of fumaric acid derivatives as NF-kappaB inhibitors and the treatment of diseases influenced by NF-kappaB (Abstract)," also stating that Joshi "further disclose the fumaric acid derivative, fumaric acid diethyl ester (paragraph [0020]), used in the preparation of a pharmaceutical composition in an amount of 1 to 500 mg (paragraph [0021]); wherein the composition is administered orally and in the form of micro-tablets with an enteric coating (paragraph [0023]), encompassing claims 77-82." Action at page 4. The Examiner acknowledged that Joshi "differs from the instant claims insofar as it does not disclose treating myocardial infarction." Action at page 4.

Despite the significant differences between Pye and Joshi, and the claimed invention, the Examiner nonetheless asserted that

[i]t is *prima facie* obviousness to select a known material based on its suitability for its intended use. Also, established precedent holds that it is generally obvious to add known ingredients to known compositions with the expectation of obtaining their known function. MPEP 2144.07. Therefore, it would have been obvious to one of ordinary skill in the art to have used fumaric acid diethyl ester as the NF-kappaB inhibitor in the method of Pye et al. to treat myocardial infarction to achieve the known function of decreasing the amount of reperfusion injury motivated by the desire to use a compound known to be a NF-kappaB inhibitor as disclosed by Joshi et al.

Action at page 4.

Applicant respectfully traverses this rejection.

In order for a combination of references to render a claimed invention obvious those references together must enable the skilled artisan to practice what they are alleged to teach. *See Beckman Instruments, Inc. v. LKB Produkter AB*, 892 F.2d 1547, 1551, 13 U.S.P.Q.2d 1301, 1304 (Fed. Cir. 1989) (“[I]n order to render a claimed apparatus or method obvious, the prior art must enable one skilled in the art to make and use the apparatus or method.” The combination of Pye with Joshi does not enable the claimed methods of treatment and accordingly cannot render the pending claims obvious.

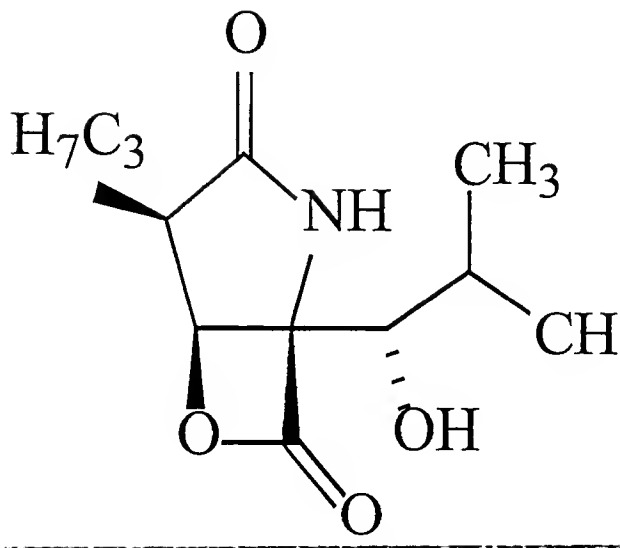
Joshi includes data showing that dimethyl fumarate inhibits TNF-induced translocation of NF-kappaB to the nucleus of cultured cells and also inhibits NF-kappaB stimulated transcription of a reporter construct. *See Examples 6 and 7 at pages 4 and 5.* Joshi also includes assertions that many diseases can be treated using the fumarate derivatives disclosed therein. However, Joshi nowhere discloses any data in any model

system for any of those diseases. The entire basis for Joshi's assertion that the compounds disclosed therein can be used to treat the diseases disclosed therein appears to be that there is some suggestion in the art that the NFkB may be involved in those diseases. That is not enough to enable the use of the compounds disclosed in Joshi for the treatment of the diseases disclosed in Joshi, *as the Office has already concluded*.

Joshi corresponds to U.S. Patent Application No. 10/250,983, which has been abandoned following a final rejection of the method of treatment claims for, among other things, a lack of enablement. As reflected in that rejection, the Office concluded that the disclosure of Joshi was not sufficient to enable treatment of any disease disclosed therein by administering dimethyl fumarate or other fumarate derivatives.

Joshi does not disclose use of a fumarate derivative to treat any of the conditions recited in the pending claims. However, even if it did, Joshi could not enable such methods of treatment because Joshi does not include any data from pre-clinical models of any disease. Thus, Joshi certainly also does not enable treatment of the conditions recited in the pending claims for at least the reasons that led the Office to conclude that the claims presented during prosecution of the U.S. counterpart of Joshi are not enabled.

Pye does not remedy the lack of enablement deficiency of the Joshi reference. Pye does not even mention fumarate derivatives. Instead, the reference is directed to administration of PS-519. PS-519 has the following structure:



That structure is not similar to the structure of dimethyl fumarate or methyl hydrogen fumarate, the compounds recited in the amended claims. Accordingly, the activity of PS-519 in the pig model system discussed in Pye does not enable the pending claims.

In summary, because the Joshi and Pye references do not enable the use of the compounds recited in the amended claims for treatment of the conditions recited in the pending claims, those references do not enable the claimed invention and the invention is nonobvious over those references.

C. The Pending Claims Are Enabled

In contrast to the prior art, the specification of this application includes data reporting on the activity of dimethyl fumarate in a rat model of cardiac insufficiency (Example A at page 7 of the application publication) and salt-sensitive Dahl-rats which develop heart failure (Example D at page 8 of the application publication). Methyl hydrogen fumarate is the primary metabolite of dimethyl fumarate. Accordingly, the data described in those established models of the conditions recited in the claims demonstrates the enablement of the claimed methods of treatment using dimethyl fumarate and methyl hydrogen fumarate.

D. Conclusion


In view of the foregoing amendments and remarks, Applicant respectfully requests reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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